CASE REPORTS

Myxedema Masked by Hypoparathyroidism Following Subtotal Thyroidectomy

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HYPOTHYROIDISM AND HYPOPARATHYROIDISM are well-recognized complications of subtotal thyroidectomy.[1,2] In fact, the frequency with which both overt and latent forms are being discovered is on the increase.[3] The following case report illustrates an unusual clinical interrelationship between these two complications which has not previously been emphasized.

Report of a Case

A 25-year-old Caucasian woman was found to have thryrotoxicosis by clinical evaluation and an elevated protein-bound iodine (PBI) and radioiodine^{131} (RAI) uptake in 1966. After three months of taking propylthiouracil (Propylthiouracil®) she underwent an "80 percent subtotal thyroidectomy." Postoperatively calcium was given orally for "muscle cramps" but was discontinued after several months without recurrence of this symptom.

USP thyroid, 0.2 grams daily, was prescribed although the patient was told she was "euthyroid." Subsequently, she generally felt well but did note "excessive energy" and mild symptoms of insomnia, heat intolerance, and a tendency to lose weight, offset only by an increased appetite. Five months before her initial clinic visit with us (February 1969) she discontinued taking desiccated thyroid without the advice of a physician. She denied any change in her symptoms for the next three months; however, one to two months before being seen in our clinic she had noted the onset of tremulousness, increased perspiration, nervousness and increased insomnia, heat intolerance, and a weight loss of 10 pounds although her appetite continued to be good. Because of these symptoms she sought medical attention. The remainder of her medical history was non-contributory.

On physical examination, blood pressure was 100/75 mm of mercury, pulse 76 beats per minute, respirations 14 per minute, oral temperature 36°C (98°F), weight 112 pounds and height 60 inches. Her palms were cool, dry and normal color. Skin and hair texture were normal. No ophthalmologic abnormalities were noted. The thyroidectomy scar was well-healed, and thyroid tissue was not palpable. Results of cardiac examination were normal. A coarse tremor of both outstretched hands was present, and deep tendon reflexes were brisk but without clonus. The patient appeared hyperkinetic, but her sensorium, muscle strength, coordination, and sensation were intact. Chvostek's and Trousseau's signs were absent. The remainder of the physical examination was unremarkable.

The initial pertinent laboratory evaluation (Table 1) showed a protein bound iodine (PBI)

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Submitted March 2, 1970.

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TABLE 1.—*Results of Laboratory Examinations on Three Occasions*

TEST	NORMAL*	INITIAL (None)†	SECOND (Vitamin D & Calcium)†	FINAL (Vitamin D & Calcium & Thyroid)†
PBI (mcg per 100 ml)	3.5-8.0	5.9	8.0	....
24-hour RAI uptake	15-45%	0.8%	2.3%	....
6-hour RAI uptake	6-20%	2.7%	....	....
Resin T_3 uptake	25-35%	....	21.0%	30.0%
Cholesterol (mg per 100 ml age 20-29)	120-240	250	644	250
Calcium (mg per 100 ml)	8.5-10.5	7.0	10.7	10.5
Phosphate (mg per 100 ml)	2.5- 4.5	7.5	5.8	3.5
Alkaline Phosphatase	4-17 KAU‡	8 KAU‡	10 KAU‡	8 KAU‡
Achilles' tendon photomotogram	260-380 mm/sec	....	440 mm/sec	270 mm/sec

*Letterman General Hospital, 1969, normal laboratory values.
†Treatment regimen.
‡King-Armstrong Units

of 5.9 mcg per 100 ml, cholesterol of 250 mg per 100 ml, RAI uptake at 6 hours 2.7 percent and at 24 hours 0.8 percent. The serum calcium was 7.0 mg and phosphate 7.5 mg per 100 ml, and alkaline phosphatase 8 King-Armstrong units. Skull films were normal.

Hypoparathyroidism was considered the primary diagnosis, and calcium lactate and Vitamin D were prescribed. After three weeks of therapy the patient was significantly improved. The serum calcium rose to 10.8 mg per 100 ml and serum phosphate fell to 4.6 mg per 100 ml. However, shortly thereafter she began to notice decreased appetite, fatigue, lethargy and intolerance to cold. These symptoms progressed, and over the next four weeks the patient gained five pounds. Hoarseness developed along with eyelid puffiness, dryness of the skin, constipation, menometrorrhagia and loss of hair from the scalp, the sides of the eyebrows and the eyelashes.

At this time the pulse rate was 72, blood pressure 100/60 mm of mercury, respirations 12 per minute, temperature 36°C (98°F) and weight 117 pounds. The patient appeared myxedematous. Her skin was puffy, cool, dry and somewhat coarse. Her hair was also dry, and her eyelashes and the lateral portion of both eyebrows were almost absent. The thyroid bed remained unchanged. Although the sensorium was normal, she appeared sluggish by contrast with her hyperkinesis on earlier examination. No tremor could be detected, and the deep tendon reflexes were slowed, especially on relaxation. Muscle strength was normal.

Laboratory evaluation at this time (Table 1) showed PBI of 8.0 mcg per 100 ml, 24-hour RAI uptake of 2.3 percent, triiodothyronine uptake of 21 percent, a photomotogram of 440 mm per second and cholesterol of 644 mg per 100 ml. The serum calcium was 10.7 mg and serum phosphate 5.8 mg per 100 ml, and the alkaline phosphatase was 10 King-Armstrong units.

Hypothyroidism was diagnosed, and desiccated thyroid was added to the daily regimen of calcium and vitamin D. After one month of this therapy the symptoms completely disappeared and the patient felt well. The final laboratory evaluation (Table 1) showed that the cholesterol had fallen to 250 mg per 100 ml, the resin T_3 uptake was 30 percent and the photomotogram was 270 mm per second.

Discussion

The initial diagnosis of thyrotoxicosis in 1966 seems justified. However, the data available to justify the diagnosis of hypoparathyroidism in the early postoperative period are inadequate, although the history suggests that at least transient hypoparathyroidism did exist and was treated briefly. Full thyroid replacement therapy was prescribed postoperatively but without documentation of the functional status of the thyroid gland at that time.

When the patient was first seen by us she was not receiving any medication. Five months previously she had voluntarily stopped taking desiccated thyroid, and three years previously, a few months after operation, the calcium had been discontinued. Our initial clinical impression included hypoparathyroidism and either euthyroidism or recurrent hyperthyroidism. The laboratory data confirmed the diagnosis of hypoparathyroidism. The thyroid function tests, however, suggested either normal thyroid function (PBI) or hypothyroidism (6 and 24-hour RAI uptake). At that time, if the low RAI uptake indicated hypothyroidism, it was not apparent clinically.

The clinical situation became clearer, however, when shortly after correction of the hypoparathyroidism with calcium and vitamin D, florid hypothyroidism developed. RAI uptake remained low (Table 1, second determination) and the resin T_3 uptake, photomotogram and sharply elevated serum cholesterol confirmed the diagnosis of hypothyroidism. However, the PBI remained normal.

In retrospect, it seems likely that the patient had been hypothyroid since discontinuation of the thyroid replacement therapy more than five months earlier, but that the early signs and symptoms of hypothyroidism were masked by the development of clinical hypoparathyroidism. The unlikely possibility remains that the myxedema developed rapidly *de novo* just after and coincidental with the correction of the hypoparathyroidism. The simultaneous existence of both hypoparathyroidism and hypothyroidism, with the former masking the latter, however, seems more likely. In fact, the symptoms related to the hypoparathyroidism suggested hyperthyroidism rather than hypothyroidism. The initial very low RAI uptake was clearly valid and was evidence of the existence of the hypothyroid state at the time hypoparathyroidism was diagnosed. The normal PBI throughout remains difficult to explain. In mild hypothyroidism an overlap of the PBI into the low normal range is reported in about 5 percent of cases. In obviously myxedematous patients, however, the PBI is almost always low, usually below 2.5 mcg per 100 ml. Besides thyrotoxicosis, causes of an unexpectedly elevated PBI include exogenous iodine, inactive iodoproteins usually released during thyroiditis, estrogen therapy, pregnancy, and thyroid replacement with pure tetraiodothyronine (T_4).[4] Laboratory error, of course, is a factor that also must be kept in mind. Contamination with exogenous iodine seems most likely to be responsible for the "normal PBI." In these circumstances, a serum thyroxine determination is probably a better test than the PBI. However, no history of exposure to organic or inorganic iodine could be obtained.

One final feature in this patient's clinical course is also of interest. Initially the serum cholesterol was 250 mg per 100 ml, which is slightly elevated for her age group and although usually somewhat higher, was consistent with the diagnosis of hypothyroidism. Subsequently, over a period of approximately six weeks the serum cholesterol rose to 644 mg per 100 ml and values in this range were confirmed on repeated testing. The reason for the rapid rise, however, is unclear. Perhaps this simply represents metabolically an accelerated phase in the clinical course of hypothyroidism. Since this pronounced rise in serum cholesterol did not occur until after the serum calcium had returned to normal, an intriguing possibility is that there could be a requirement for normal calcium metabolism to generate hypercholesterolemia in one who has hypothyroidism. This, of course, is only conjecture. In fact, the available information in the literature on the relationship of serum calcium to serum cholesterol suggests just the opposite effect: oral calcium supplementation may have a hypocholesterolemic action.[5] The circumstances in these reported studies, however, were different than in the present situation and, so far as we can determine, the relation between calcium and cholesterol metabolism in hypothyroidism has not been studied.

Summary

Two complications of subtotal thyroidectomy, clinical hypoparathyroidism masking the recognition of myxedema were encountered in a 25-year-old white woman who had undergone subtotal thyroidectomy three years before. Only after the correction of the former did the diagnosis of the latter become apparent. The simultaneous occurrence of these two conditions following subtotal thyroidectomy may well be more common than is being recognized.

TRADE AND GENERIC NAMES OF DRUGS

Propylthiouracil® . . . . propylthiouracil, calcium, vitamin D, thyroid

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—WAYNE TOBIN, M.D., Miami

Extracted from *Audio-Digest Internal Medicine,* Vol. 16, No. 11, in the Audio-Digest Foundation's subscription series of tape-recorded programs. For subscription information: 619 S. Westlake Ave., Los Angeles, Ca. 90057.